

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-9. (Canceled)

10. (Previously presented) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with non-insulin dependent diabetes mellitus (NIDDM), comprising:

administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1, thereby treating impaired glucose tolerance.

11. (Original) The method of claim 10 wherein the receptor binding compound is selected from (a) a peptide which comprises the amino acid sequence of glucagon-like peptide-1, and (b) a variant peptide comprising an amino acid sequence that differs from the sequence of glucagon-like peptide-1 by one or more substitutions, deletions or insertions.

12. (Original) The method of claim 11 wherein the receptor binding compound is glucagon-like peptide-1.

13. (Previously presented) The method of claim 11 wherein the receptor binding compound is glucagon-like peptide-1 (7-37) which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly SEQ ID NO:3.

14. (Previously presented) The method of claim 11 wherein the receptor binding compound is glucagon-like peptide-1 (7-36) amide which has the sequence His

Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe
Ile Ala Trp Leu Val Lys Gly Arg (NH₂) SEQ ID NO:4.

15. (Original) The method of claim 11 wherein the receptor binding compound is a variant peptide in which the combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than ten amino acids from the amino acid sequence of glucagon-like peptide-1.

16. (Original) The method of claim 10 wherein the receptor binding compound is expressed by a polynucleotide.

17. (Previously presented) The method of claim 10 wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000 daltons.

18. (Previously presented) The method of claim 10 wherein the step of administering is selected from the group consisting of intravenous, subcutaneous, intramuscular, intraperitoneal, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.

19. (Original) The method of claim 10, further comprising administering an agent that enhances the half-life in vivo of said receptor binding compound.

20. (Original) The method of claim 19 wherein the agent is administered concurrently with the composition.

21. (Original) The method of claim 19 wherein the agent is covalently linked to the receptor binding compound.

22. (Original) The method of claim 18 wherein intravenous administration is in a dose range of from about 0.3 to about 2.0 pmol/kg per minute.

23. (Original) The method of claim 18 wherein continuous subcutaneous administration is in a dose range of from about 1.0 to about 20.0 pmol/kg per minute.

24. (Currently Amended) The method of claim 10, wherein said composition contains an amount of said compound effective to retard or arrest the loss of plasma glucose control or the development of non-insulin dependent diabetes mellitus.

25. (Original) The method of claim 24 wherein the receptor binding compound is selected from (a) a peptide which comprises the amino acid sequence of glucagon-like peptide-1, and (b) a variant peptide comprising an amino acid sequence that differs from the sequence of glucagon-like peptide-1 by one or more substitutions, deletions or insertions.

26. (Original) The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1.

27. (Previously presented) The method of claim 25 wherein the receptor binding compound is glucagon-like peptide-1 (7-37) which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly SEQ ID NO:3.

28. (Previously presented) The method of claim 25 wherein the receptor binding compound is a glucagon-like peptide-1 (7-36) amide which has the sequence His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg (NH₂) SEQ ID NO:4.

29. (Original) The method of claim 25 wherein the receptor binding compound is a variant peptide in which the combination of the substitutions, deletions and insertions in the amino acid sequence does not differ by more than five amino acids from the amino acid sequence of glucagon-like peptide-1.

30. (Original) The method of claim 24 wherein the receptor binding compound is expressed by a polynucleotide.

31. (Previously presented) The method of claim 24 wherein the receptor binding compound is an organic molecule having a molecular weight of not greater than about 5000 daltons.

32. (Previously presented) The method of claim 24 wherein the step of administering is selected from the group consisting of intravenous, subcutaneous, intramuscular, intraperitoneal, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.

33. (Original) The method of claim 32 wherein intravenous administration is in a dose range of from about 0.1 to about 10.0 pmol/kg per minute.

34. (Original) The method of claim 32 wherein continuous subcutaneous administration is in a dose range of from about 0.1 to about 75.0 pmol/kg per minute.

35. (Previously presented) The method of claim 10, wherein said composition contains an amount of said compound effective to improve entrainment of β -cell insulin secretory responses the exogenous glucose oscillations.

36. (Previously presented) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with NIDDM comprising:

administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1, said composition containing an amount of said compound effective to enhance a normalization of insulin secretory patterns in impaired glucose tolerance, thereby treating impaired glucose tolerance.

37. (Previously presented) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with NIDDM comprising:

administering to said individual a compound which binds to a receptor for glucagon-like peptide-1, said composition containing an amount of said compound effective to reduce plasma insulin levels in an individual with impaired glucose tolerance, thereby treating impaired glucose tolerance.

38. (Previously presented) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with NIDDM comprising:

administering to said individual a composition comprising a compound which binds to a receptor for glucagon-like peptide-1, said composition containing an amount of said compound effective to reduce insulin resistance in an individual with impaired glucose tolerance, thereby treating impaired glucose tolerance.

Claims 39 and 40 (Canceled)

41. (Previously presented) The method according to claim 10, wherein said composition contains an amount of said compound effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.

Claims 42 and 43 (Canceled)

44. (Currently Amended) A method for treating an individual with impaired glucose tolerance who has not been diagnosed with non-insulin dependent diabetes mellitus (NIDDM), comprising:

administering to said individual a composition comprising an exendin ~~or a variant of said exendin comprising an amino acid sequence that differs from the sequence of exendin by one or more substitutions, deletions or insertions~~, thereby treating impaired glucose tolerance.

45. (Previously presented) The method of claim 44 wherein the exendin is exendin 3, SEQ ID NO:7.

46. (Previously presented) The method of claim 44, wherein the exendin is exendin 4, SEQ ID NO:9.

47. (Canceled)

48. (Previously presented) The method of claim 44, wherein the step of administration is selected from the group consisting of intravenous, subcutaneous, intramuscular, intraperitoneal, injected depot with sustained release, deep lung insufflation with sustained release, buccal or patch.

49. (Currently Amended) The method of claim 44, wherein the exendin ~~or variant thereof~~ is administered in a range of 0.005 nmol/kg to 20 nmol/kg.

50. (Currently Amended) The method of claim 44, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.

51. (Currently Amended) The method of claim 44, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to retard or arrest the loss of plasma glucose control or the development of non-insulin dependent diabetes mellitus.

52. (Currently Amended) The method of claim 44, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to enhance a normalization of insulin secretory patterns in impaired glucose tolerance.

53. (Currently Amended) The method of claim 44, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to reduce plasma insulin levels in an individual with impaired glucose tolerance.

54. (Currently Amended) The method of claim 44, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to reduce insulin resistance in an individual with impaired glucose tolerance.

55. (Currently Amended) A method for reducing a risk of cardiovascular event comprising:
administering to an individual a composition comprising an exendin ~~or a variant thereof~~, thereby reducing the risk of a cardiovascular event.

56. (Currently Amended) The method of claim 55, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.

57. (Currently Amended) A method for reducing a risk of a cerebrovascular event comprising:
administering to an individual a composition comprising an exendin ~~or a variant thereof~~, thereby reducing the risk of a cerebrovascular event.

58. (Currently Amended) The method of claim 57, wherein said composition contains an amount of the exendin ~~or variant thereof~~ effective to enhance the regularity of insulin responses, or the amplitude thereof, in reaction to changes in plasma glucose.